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Lipid Treatment News

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New National Cholesterol Education Program Guidelines

The most recent National Cholesterol Education Program guidelines, developed by the Adult Treatment Panel III, (ATP III) were released in May 2001 (1). These guidelines were the first update by this panel since the ATP II report released in 1993. In general, the new guidelines are more aggressive in selection of patients for intervention and the degree of intervention recommended. Based on data from the Third Annual National Health and Nutrition Survey, the number of Americans who could qualify for lipid lowering drug therapy by these guidelines is estimated to increase to 36 million, from approximately 15 million eligible under the ATP II guidelines (2). This recommendation is controversial and has generated concern about the significant increase in potential costs to the health care system.

ATP III guidelines recommend a goal LDL cholesterol of less than 100 mg/dl not only for patients with CHD, but also for those with CHD risk equivalents, a significant change from ATP II. CHD risk equivalents are factors that confer a degree of risk for experiencing a CHD event similar to that of individuals with known CHD. These risk equivalents are diabetes mellitus, any form of atherosclerotic disease (including symptomatic carotid artery disease, abdominal aortic aneurysm, and peripheral arterial disease) and multiple risk factors that confer a 10 year risk of CHD that is greater than 20%. Ten-year risk of CHD is estimated using a risk assessment tool derived from the Framingham data that is based on total cholesterol, age, smoking status, HDL concentration, and systolic blood pressure (1).

The recommendation for a LDL-C goal of less than 100 mg/dl is based on indirect evidence from epidemiological and angiographical studies. Outcome studies designed to identify the optimal LDL goal have not yet been completed, and data from existing studies are conflicting in demonstrating the benefit of aggressive lipid lowering. Analysis of data from angiographical trials seemed to indicate that patients who have LDL-C less than 100 mg/dl had more regression of lesions, less progression and a trend toward fewer coronary events. The data from large-scale outcome trials, however, do not confirm this finding. In fact, some studies suggest there is no benefit to LDL lowering with statin drugs in patients with a history of myocardial infarction or unstable angina whose LDL is less than 125 –135 mg/dl at baseline (3,4) and that there is no additional benefit seen if LDL is lowered below 125 mg/dl (5). Other experts describe these data as a statistical anomaly, making this is a controversial issue.

ATP III further refines recommendations for LDL cut-points at which to initiate therapeutic lifestyle changes and drug therapy (Table 1). It is recommended that drug therapy be considered at lower LDL concentrations in secondary prevention and high-risk primary prevention. The value at which HDL is considered low is increased from <35 mg/dl to <40 mg/dl. Triglyceride classification cut-points have been redefined to reflect their role in the metabolic syndrome. The metabolic syndrome is characterized by abdominal obesity, atherogenic lipoprotein profile (elevated triglyceride, small dense LDL, and decreased HDL), hypertension, insulin resistance, and prothrombotic and proinflammatory states. Treatment is primarily based on weight reduction, increased activity, and treatment of risk factors such as hypertension and dyslipidemia.

Table 1 - ATP III LDL Treatment Decision Cut-points(1)

Risk Category	LDL Goal (mg/dl)	Initiate Therapeutic Lifestyle Changes (mg/dl)	Consider Drug Therapy (mg/dl)
CHD or CHD Risk Equivalents (10-year risk >20%)	<100	≥100	≥130 (100–129: drug optional)
2+ Risk Factors (10-year risk <20%)	<130	≥130	10-year risk 10–20%: ≥130 10-year risk <10%: ≥160
0–1 Risk Factor	<160	≥160	≥190 (160–189: LDL-lowering drug optional)

Statins and myositis

The recent market withdrawal of cerivastatin (Baycol®) highlights one of the most potentially severe adverse events attributed to statin therapy. Myositis, characterized by muscle pain and weakness and creatine phosphokinase elevations of 10 times normal, can in extreme cases lead to rhabdomyolysis and death. Cerivastatin was implicated in a significantly greater number of cases of myositis and rhabdomyolysis than had been reported with other statin drugs. While the risk factors for experiencing myositis are not well defined, statin dose, drug interactions and hypothyroidism are important.

Two types of drug interactions are seen. Pharmacokinetic interactions between statins that are metabolized by the cytochrome P450 3A4 pathway and drugs that inhibit these enzymes result in elevations of the plasma concentrations of lovastatin, simvastatin, and atorvastatin. The second mechanism is a pharmacodynamic interaction between statins and other lipid lowering agents which may also by themselves cause myositis. Most notable of these is gemfibrozil, while fenofibrate and niacin are less commonly reported to cause clinically significant muscle symptoms. Some reports have indicated that the relationship between cerivastatin and gemfibrozil may have included both types of interactions.

Table 2 - Drug Selection by Lipoprotein Profile

Lipoprotein Profile	Recommended Drug Treatment
Elevated LDL only	1) Statin 2) Resin 3) Niacin
Elevated LDL, TG	1) Niacin 2) Statin 3)Fenofibrate
Elevated TG	1) Niacin 2) Gemfibrozil 3) Fenofibrate 4) Omega 3 Fatty Acids*

*not FDA approved for lipid lowering

Drug selection

Data from large scale outcome trials support the use of statins as first line therapy for secondary prevention in most patients (3,5,6). The choice of statin should take into consideration the patient's history of intolerance to a particular statin, the percent LDL lowering required to reach goal, the

potential for drug interactions as previously described and the cost per LDL lowering.

Individuals with CHD and isolated low HDL may benefit from gemfibrozil (7). There are no outcome studies designed to specifically evaluate the effects of triglyceride lowering in reducing risk of cardiovascular events. Treatment may be further based on lipoprotein abnormalities (Table 2). While statins do lower modestly elevated triglycerides, they are less effective than fibric acid derivatives and niacin and should not be used as first line therapy.

Table 3 – Comparative Cost of Therapy

Brand Name	Generic Name	Tablet Strength	Dose	Cost / 30-days#
20-26% LDL Reduction				
NIACIN	NIACIN IR	500MG	TID	$16.30
LIPITOR^ ✂	ATORVASTATIN	10MG	½ T QHS	$28.10
ZOCOR ✂	SIMVASTATIN	10MG	½ T QHS	$30.80
LOVASTATIN*	LOVASTATIN	10MG	QPM	$34.90
MEVACOR	LOVASTATIN	10MG	QPM	$38.75
LESCOL	FLUVASTATIN	20MG	QHS	$40.00
ZOCOR	SIMVASTATIN	5MG	QHS	$48.70
PRAVACHOL	PRAVASTATIN	10MG	QHS	$57.00
CHOLESTYRAMINE	CHOLESTYRAMINE	4GM	BID	$73.60
COLESTID	COLESTIPOL	5GM	BID	$97.45
COLESTID	COLESTIPOL	1GM	4T BID	$100.30
WELCHOL	COLESEVELAM HCL	625MG	3T BID	$147.65
27-33% LDL Reduction				
LIPITOR^ ✂	ATORVASTATIN	10MG	½ T QHS	$28.10
LESCOL	FLUVASTATIN	40MG	QHS	$41.50
ADVICOR	LOVASTATIN / NIACIN	20-1000MG	QPM	$49.30
PRAVACHOL	PRAVASTATIN	20MG	QHS	$57.80
LOVASTATIN	LOVASTATIN	20MG	QPM	$60.55
ZOCOR	SIMVASTATIN	10MG	QHS	$61.60
MEVACOR	LOVASTATIN	20MG	QPM	$62.40
34-40% LDL Reduction				
LIPITOR ✂	ATORVASTATIN	20MG	½ T QHS	$43.70
LESCOL XL	FLUVASTATIN	80MG	QHS	$50.15
LIPITOR	ATORVASTATIN	10MG	QHS	$56.25
ADVICOR	LOVASTATIN / NIACIN	20-750MG	2T QPM	$92.40
PRAVACHOL	PRAVASTATIN	40MG	QHS	$100.85
ZOCOR	SIMVASTATIN	20MG	QHS	$108.40
LOVASTATIN	LOVASTATIN	40MG	QPM	$111.80
MEVACOR	LOVASTATIN	40MG	QPM	$122.70
41-47% LDL Reduction				
LIPITOR ✂	ATORVASTATIN	40MG	½ T QHS	$48.15
LIPITOR	ATORVASTATIN	20MG	QHS	$87.35
ADVICOR	LOVASTATIN / NIACIN	20-1000MG	2T QPM	$98.70
ZOCOR	SIMVASTATIN	40MG	QHS	$113.20
LOVASTATIN	LOVASTATIN	40MG	2T QPM	$223.55
MEVACOR	LOVASTATIN	40MG	2T QPM	$245.35
48-54% LDL Reduction				
LIPITOR ✂	ATORVASTATIN	80MG	½ T QHS	$47.55
LIPITOR	ATORVASTATIN	40MG	QHS	$96.30
ZOCOR	SIMVASTATIN	80MG	QHS	$114.70
55-60% LDL Reduction				
LIPITOR	ATORVASTATIN	80MG	TABLET	$95.10
Elevated Triglycerides				
NIACOR	NIACIN	500MG	TID	$16.30
TRICOR	FENOFIBRATE	67MG	QHS	$21.75
GEMFIBROZIL	GEMFIBROZIL	600MG	BID	$51.25
TRICOR	FENOFIBRATE	160MG	QHS	$67.45
LOPID	GEMFIBROZIL	600MG	BID	$77.10

✂ Using ½ tablets can reduce cost of therapy by 50% and preserve medical outcomes (8)
T = Tablet
# Costs reflect AWP – 13% on 3/7/02
* Lovastatin is the first generic in the class
^ Low doses of atorvastatin are comparable to intermediate or high doses of other statins. Although the tablets are not scored, they break easily. Many patients can be started at 5mg (1/2 of a 10 mg tablet) though it is not an FDA approved dose.

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The OHP Practitioner-Managed Prescription Drug Plan: Opportunities for Clinician Involvement

The Health Resources Commission (http://www.ohppr.state.or.us/) has selected the next four drug classes to evaluate for inclusion on the Practioner-Managed Prescription Drug Plan (PMPDP). The four drug classes selected were: angiotensin converting enzyme inhibitors and agngiotensin receptor blockers, calcium channel blockers, estrogens, and acute migraine drugs.

Subcommittees are being formed to review a class and make recommendations to the HRC. Subcommittee composition will include physicians, pharmacists, other health care providers and consumer interests. Volunteers interested in participating on one of these subcommittees should contact Kelley Cullison at kelley.cullison@state.or.us or (503) 378-2422 Ext. 227 as soon as possible.

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